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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,400	07/22/2002	Thomas Hantke	0480/01219	2952

26474 7590 11/13/2008

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EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
11/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/088,400	HANTKE ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,8,10,11,13-16,20-22 and 26-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6,8,10,11,13-16,20-22 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted August 1, 2008 is acknowledged.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1, 2, 4, 6, 8, 10, 11, 13-16, 20-22, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andries et al. (US 6,197,779), in view of Goertz et al. (US 4,801,460), Nakamichi et al. (US 5,456,923), Sasatani et al. (US 5,876,760) and Takada (US 5,350,741), and in further view of Baert (EP 0 872 233, IDS)

3. Andries et al. teaches the HIV inhibiting pyrimidine derivatives herein and the method of using the same for preparing pharmaceutical composition, and for treating HIV infection. See, the abstract, cols 1-10, 17-19. The elected compound herein is a preferred compound disclosed by Andries et al. see, col. 10, lines 14-15. The compounds may be formulated into various conventional dosage forms, such as powders, tablet, capsule with solid carrier and other pharmaceutical excipients. See, particularly, col. 18, line 19 to col. 19, line 25. (Applicants also admitted the compounds are known in the art, citing PCT/EP99/02043, which is equivalent to US 6,197,779, and PCT EP/02044, see page 2 herein)

4. Andries et al. do not teach expressly the particular dosage form herein with PVP or it's copolymer as carrier and polyoxyethylene hydrogenated castor oil and citric acid as additional excipients, or the particular release forms.

5. However, Goertz et al. teach a solid pharmaceutical form wherein polyvinylpyrrolidone or copolymer of vinylpyrrolidone and vinyl acetate or used as carrier, and a solid solution of the active ingredient is formed. See particularly, the abstract, col. 3, lines 3-31, col. 4, lines 11-45, and the claims. There is no particular limitation as to the active ingredients employed therein. The concentration of active ingredients may be in the rage from 0.1 to 95%, with preferred range of 30-70%. 45 to 50% of polymer is used in the particular examples. Other known pharmaceutical excipients may be added accordingly. The forms may be made by extrusion. See, cols. 3-8. Nakamichi et al. teach that solid dispersion or solution is known to be useful for controlling the rate of release of a drug from dosage form or improving the bioavailability of drugs. Nakamichi et al. further teaches that other polymeric material, such as modified cellulose (e.g. hydroxypropylmethylcellulose) are similarly useful (like PVP) as solid carrier, and extrusion is a conventional method for making a solid dispersion or solution form. See, particularly, cols. 1-2, and the claims. Both Sasatani et al. and Takada teaches that polyethylene glycol castor oil ester and citric acid are known pharmaceutical excipients and are particularly known to be useful in solid form wherein Polyvinypyrrolidone is carrier. See, particularly, col. 5, lines 33-63 in Sasatani et al. and the claims in Takada.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form,

wherein vinypyrrolidone polymer or copolymer is the carrier, and with additional other pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil, citric acid.

A person of ordinary skill in the art would have been motivated to formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form, wherein vinypyrrolidone polymer or copolymer is the carrier, and with additional other pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil, citric acid, because polymeric carrier, such as vinylpyrrolidone polymer or copolymer, are known to produce solid dispersion or solution with a drug which provide controlled release and enhanced bioavailability. Further, the employment of various pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil (surfactants), and citric acid (acids), accordingly is within the skill of artisan. The further employment of other polymers, such as hydroxypropylmethylcellulose, would have been obvious since the modified cellulose is known to be similarly useful as a solid carrier. Attention is directed to Baert, which teaches the employment of combination of PVP and hydroxypropyl methylcellulose as carrier for controlled release antiviral dosage form. See, particularly, the example (pages 6-7) and the claims. Furthermore, the optimization of a result effective parameter, e.g., drug releasing profile, or the effective amounts of the drug and the other ingredients therein, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215.

> The employment of a dosage form known to be useful for a particular purpose, in a pharmaceutical package useful for the same purpose is considered within the skill of the artisan. Further, the optimization of a dosage regimen for the administration of a dosage form is considered within the skill of the artisan, absent evidence to the contrary.

6. Claim 26, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andries et al. (US 6,197,779), in view of Goertz et al. (US 4,801,460), Nakamichi et al. (US 5,456,923), Sasatani et al. (US 5,876,760) and Takada (US 5,350,741), and in further view of Baert (EP 0 872 233, IDS) for reason discussed above, and in further view of Jones et al.

Andries et al. Goertz et al. (US 4,801,460), Nakamichi et al. (US 5,456,923), Sasatani et al. (US 5,876,760), Takada (US 5,350,741), and Baert et al. do not teach expressly the particular K value of the polyvidone. It is noted that Kollidon VA64 is used in the solo example herein (page 14). It is reasonably believed that Kollidon VA64 meets the limitation of K value. Jones teaches polymers, such as Kollidon K30 and K90 and Kollidon VA 64, are particularly suitable as binder in antiviral composition for extrusion and formulation of particles. See, particularly, col. 3, lines 56 to col. 4, line 2. Therefore it would have been obvious to use those well-known polyvidone for formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form.

Response to the Arguments

Applicants' amendments and remarks submitted August 1, 2008 have been fully considered, but are not persuasive with respect to the rejections set forth above.

7. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). As evidenced in the rejection, all the elements recited herein are known in the art, and their employment herein produces nothing but predictable results. As shown in the rejection, the active ingredient herein is known to be

formulated various dosage form; the particular polymers herein are well-known pharmaceutical carriers, particularly useful as rate-controlled carriers. The melt, extruding method for producing the particle is well known, the other excipients herein are also known.

8. The evidence of record shows that the subject matter as claimed is a combination of known components selected for their known properties. A claim which unites elements with no change in their respective functions to yield a predictable result is not patentable in the absence of secondary considerations.

For over a half century, the [Supreme] Court has held that a "patent for a combination which only unites old elements with no change in their respective functions ...obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152 [87 USPQ 303] (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.

KSR Int'l v. Teleflex Inc., 82 USPQ2d 1385, 1395 (2007).

No explicit teaching is necessary to have led the skilled worker to the particular components recited in claims because each was known in the prior art, prompting the skilled worker to have combined them.

The examiner further contend that he does not the employ a per se ruler for the rejections set forth above, but considers the nature of the invention, and all the fact presented on the record. As shown by the cited references, the employment of the polymers herein, particularly their combination, are well known in the art for controlled release purpose. Applicants' arguments about pick and choose, citing Akzo v. U.S. International Trade Commission, USPQ2d are unpersuasive. Akzo is inapplicable herein. In Akzo, the claim at issue has limitations that the prior art provides no particular guidance, direction or suggestion to reach, such as the specific

polyamide and its viscosity, the concentration of sulfuric acid, the viscosity and concentration of the polymer solution. There are unpredictable or unknown features residing in the particular polymer that make the polymer particularly suitable for the process claimed. See Akzo 1244, 1245. The claim would have not been reached without picking and choosing the elements disclosed in the prior art. In instant case, the claims encompass broadly compounds defined by the general formula herein. The prior art have provided the guidance, direction and/or suggestion to all the limitation recited herein, and there is no evidence on the record showing that the active agents encompassed herein have any futures that make them distinct with respect to the controlled release formulation.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1617